

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference J 10030 PCT	<b>FOR FURTHER ACTION</b>	See item 4 below
International application No. PCT/EP2005/003163	International filing date ( <i>day/month/year</i> ) 24 March 2005 (24.03.2005)	Priority date ( <i>day/month/year</i> ) 24 March 2004 (24.03.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant JERINI AG		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

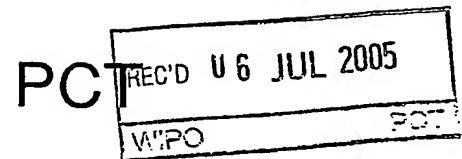
- |                                     |              |   |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the report   |
| <input type="checkbox"/>            | Box No. II   | Priority  |
| <input checked="" type="checkbox"/> | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention  |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited   |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application  |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application   |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

<p style="text-align: center;">The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 338 82 70</p>	<p>Date of issuance of this report 26 September 2006 (26.09.2006)</p> <hr/> <p>Authorized officer</p> <p style="text-align: center; font-weight: bold;">Agnes Wittmann-Regis</p> <p>e-mail: pt06@wipo.int</p>
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# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY



To:

see form PCT/ISA/220

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/EP2005/003163

International filing date (day/month/year)  
24.03.2005

Priority date (day/month/year)  
24.03.2004

International Patent Classification (IPC) or both national classification and IPC  
C07D401/12, C07D405/14, A61K31/4439

Applicant  
JERINI AG

### 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

### 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2005/003163

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**Box No. I    Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2005/003163

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1-38; 42-78 (in part); 79,80; 81-84(in part)

because:

- ☒ the said international application, or the said claims Nos. 42-44, 81-84 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 79,80 are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☒ the claims, or said claims Nos. 1-38; 42-81 (in part) are so inadequately supported by the description that no meaningful opinion could be formed.

- ☐ no international search report has been established for the whole application or for said claims Nos.

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- ☐ has not been furnished

- ☐ does not comply with the standard

the computer readable form

- ☐ has not been furnished

- ☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2005/003163

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	39-41; 42-78(in part), 81-84(in part)
	No: Claims	
Inventive step (IS)	Yes: Claims	39-41; 42-78(in part), 81-84(in part)
	No: Claims	
Industrial applicability (IA)	Yes: Claims	39-41; 44-78(in part)
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

III-1. Present claims 1-38 relate to an extremely large number of possible compounds. The structural formula (I) contains no fixed structural element except for an unspecified ring D to which a carboxylic acid (in B), an N-containing substituent (G) and a further vaguely defined substituent A are attached via some variable spacers. Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of these compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to compounds which have a pyrrolidinyloxyacetic acid amide core structure. The search covers thus compounds according to claims 39 to 41 including the example compounds of the description.

This Opinion is thus restricted to claims 39-41 and the respective parts of claims 42-78, 81-84. Other parts are not covered.

III-2. Claims 79 and 80 are directed to a "pharmaceutical composition for use together with a method of treatment for a disease...". It is unclear whether these claims are directed to a physical entity or to a method of treatment (Art. 6 PCT). No opinion will be given on these claims.

III-3. Claims 42-44, 81-84 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**V-1. State of the art**

The following documents are considered relevant:

- D1: EP-A-1 346 982 (DAIICHI PHARMACEUTICAL CO., LTD) 24 September 2003 (2003-09-24)
- D2: US 2003/171304 A1 (HOELZEMAN G?UUM ET AL) 11 September 2003 (2003-09-11)
- D3: WO 99/37621 A (HOECHST MARION ROUSSEL DEUTSCHLAND GMBH; GENENTECH, INC; PEYMAN, ANUSC) 29 July 1999 (1999-07-29)
- D4: MILLER WILLIAM H ET AL: "Identification and in vivo efficacy of small-molecule antagonists of integrin alphavbeta3 (the vitronectin receptor)" DRUG DISCOVERY TODAY, vol. 5, no. 9, September 2000 (2000-09), pages 397-408, XP002333225 ISSN: 1359-6446

**V-2. Novelty (Art. 33(2) PCT):**

The compounds of Claims 39-42 differ from D1 i. a. in the amide part (cf. claims and example 120 in paragraph 1212 on page 278), and from D2-D4 in that these documents do not disclose pyrrolidines as core structures.

Claims 39-41 and the respective parts of claims 42-78 and 81-84 fulfil thus Art. 33(2) PCT.

**V-3. Inventive step (Art. 33(3) PCT):**

Closest prior art is seen in D1. D1 discloses integrin receptor inhibitors. The problem to be solved is thus the provision of further integrin inhibitors. The compounds of Claims 39-42 differ from D1 in the amide part, in the pyridylamino substituent and in the N-substituent at the pyrrolidine nitrogen. Although the use of C-terminal amino acids is known from e. g. D4 (see compounds in Figure 2) or D3 and the terminal aminopyridine as such from D2 (all of which deal with integrin receptor inhibitors), the compounds of

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

**PCT/EP2005/003163**

claims 39-41 are not considered to represent an obvious solution to the stated problem since the way of attachment and the modification of the N-substituent is not suggested.

Claims 39-41 and the respective parts of claims 42-78 and 81-84 fulfil thus Art. 33(3) PCT.